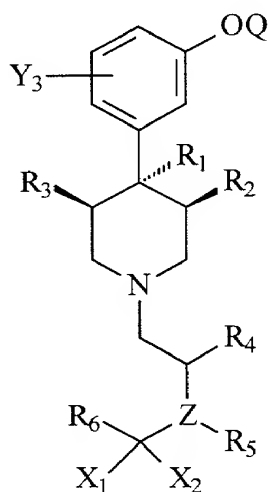


Claims:

1. A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

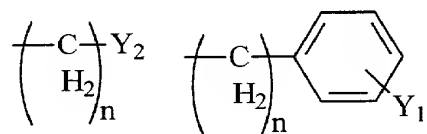
administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):

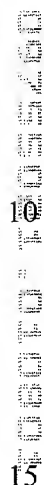


(I)

wherein Q is H or COC<sub>1-8</sub> alkyl;

R<sub>1</sub> is C<sub>1-8</sub> alkyl, or one of the following structures:





5

Y<sub>3</sub> is H, OH, Br, Cl, F, CN, CF<sub>3</sub>, NO<sub>2</sub>, N<sub>3</sub>, OR<sub>8</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

R<sub>3</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>

wherein R<sub>2</sub> and R<sub>3</sub> may be bonded together to form a C<sub>2-8</sub> alkyl group;

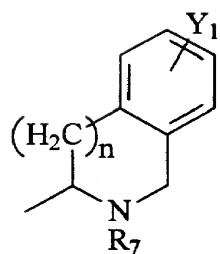
R<sub>4</sub> is hydrogen, C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkylaryl substituted by one or more groups Y<sub>1</sub>, CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub> or CO<sub>2</sub>C<sub>1-8</sub> alkyl;

$Z$  is N, O or S; where  $Z$  is O or S, there is no  $R_5$

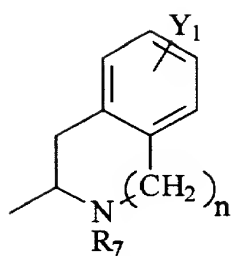
R<sub>5</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, CH<sub>2</sub>CO<sub>2</sub>C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>;

$n$  is 0, 1, 2 or 3;

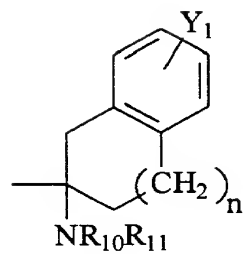
R<sub>2</sub> is a group selected from the group consisting of structures (a)-(bbb):



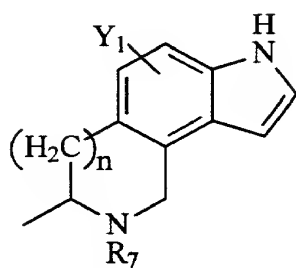
(a)



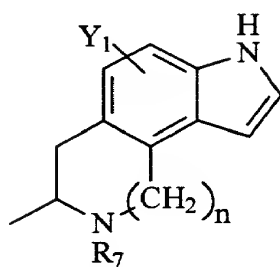
(b)



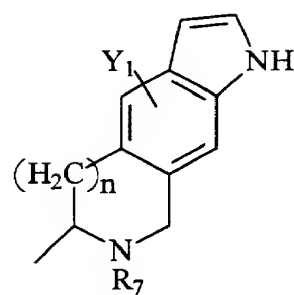
(c)



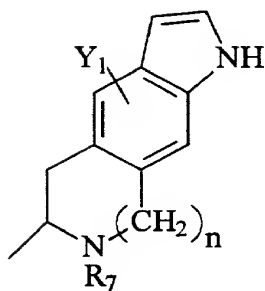
(d)



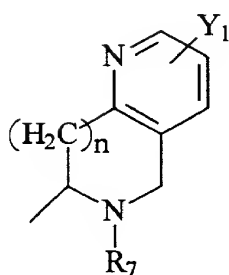
(e)



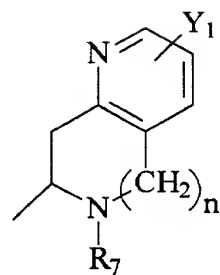
(f)



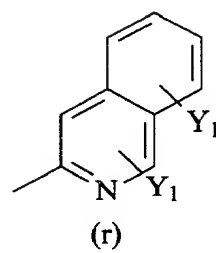
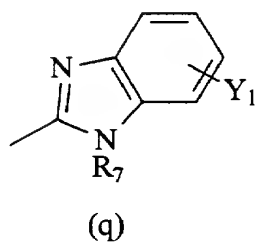
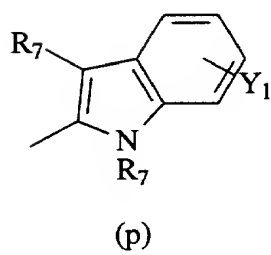
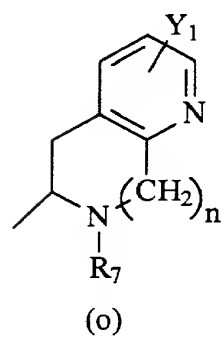
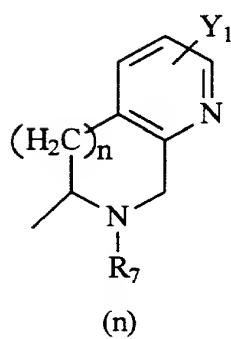
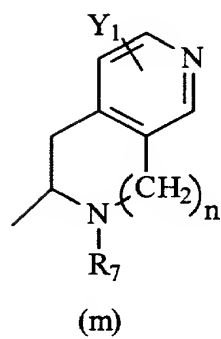
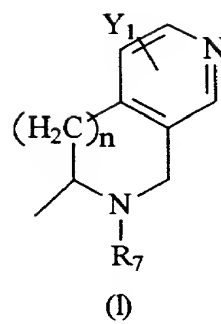
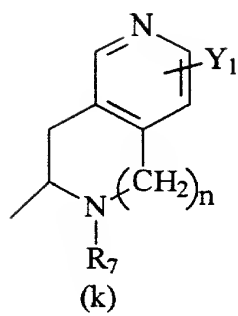
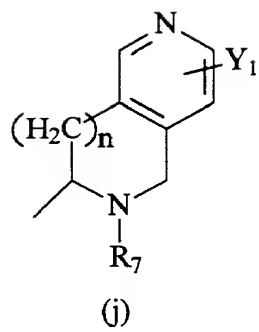
(g)

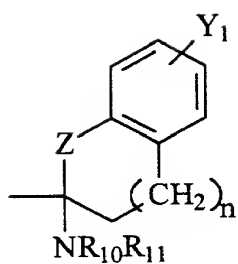


(h)

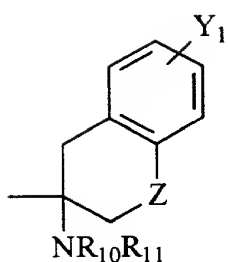


(i)

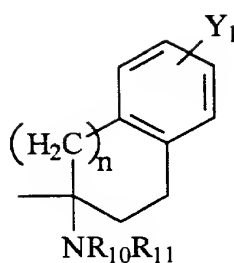




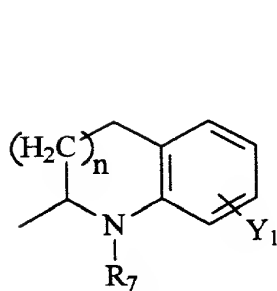
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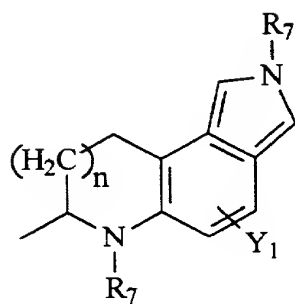
(t)



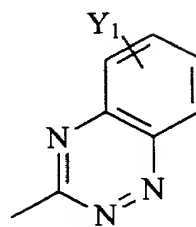
(u)



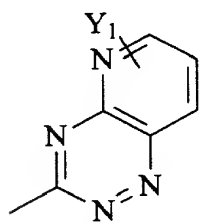
(v)



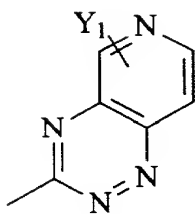
(w)



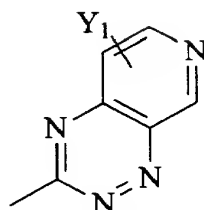
(x)



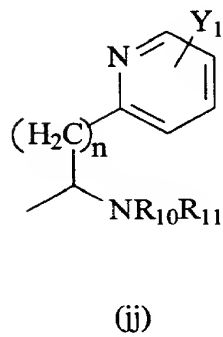
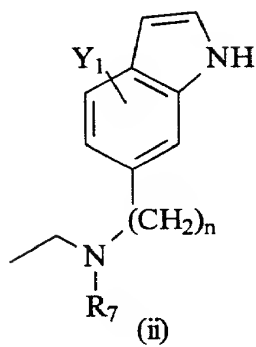
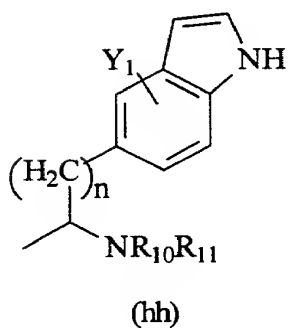
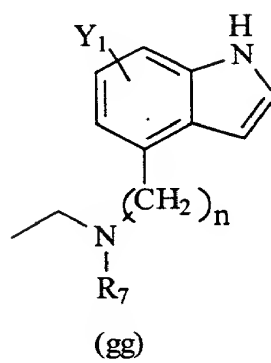
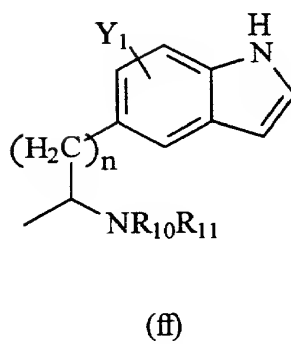
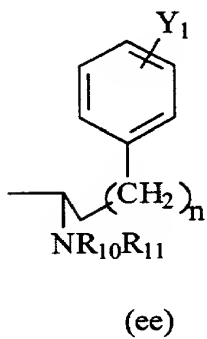
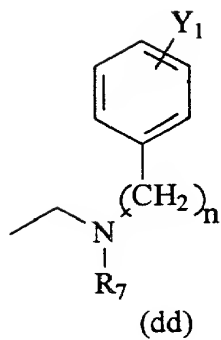
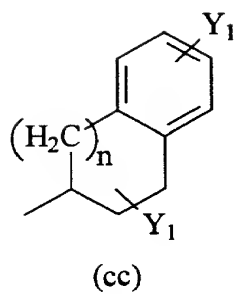
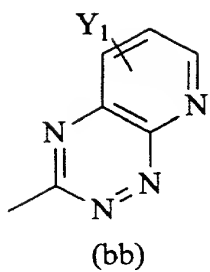
(y)

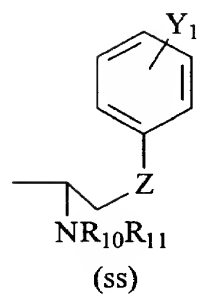
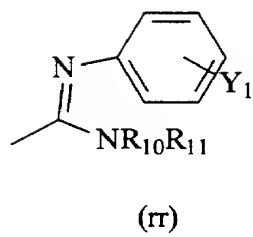
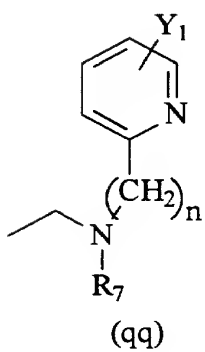
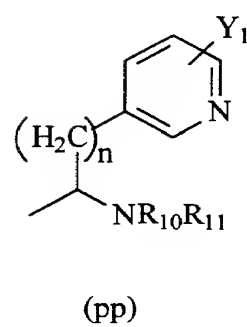
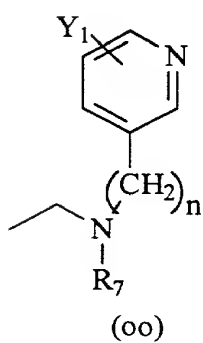
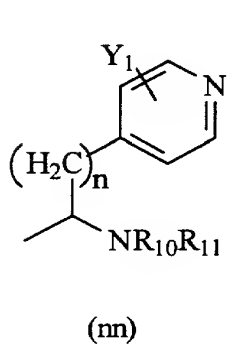
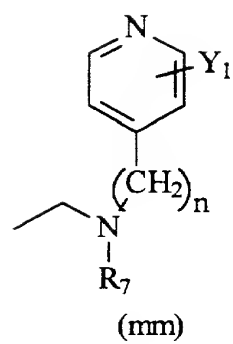
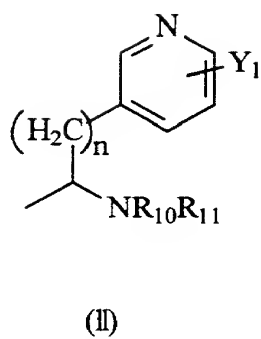
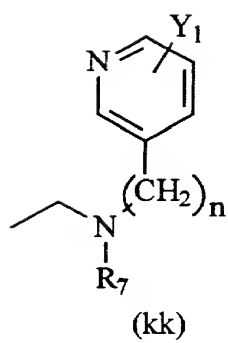


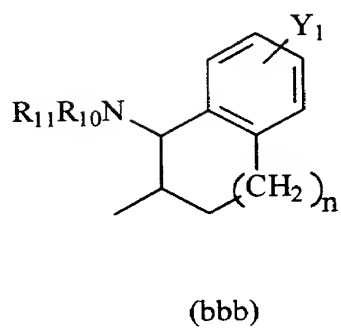
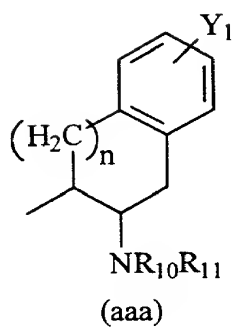
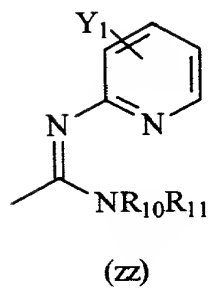
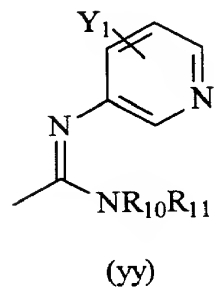
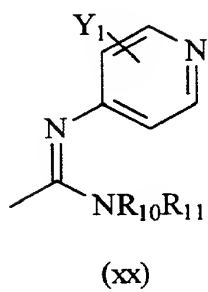
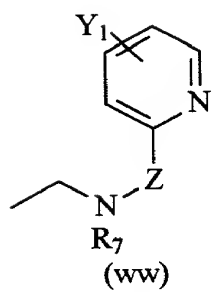
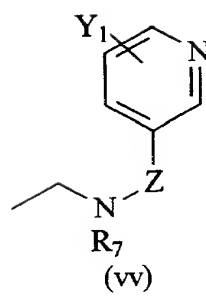
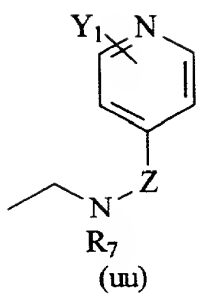
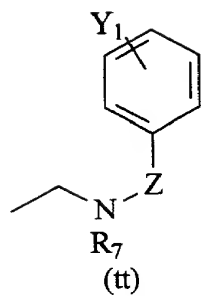
(z)



(aa)









X<sub>1</sub> is hydrogen, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl;

X<sub>2</sub> is hydrogen, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl;

or X<sub>1</sub> and X<sub>2</sub> together form =O, =S, =NH;

R<sub>7</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>,

5 NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>, C(=NH)NR<sub>16</sub>R<sub>17</sub>.

R<sub>8</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CONR<sub>13</sub>R<sub>14</sub>,

CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>9</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

R<sub>10</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

10 R<sub>11</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>12</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>13</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>14</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>15</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>16</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

and

R<sub>17</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>

2. The method of claim 1, wherein said kappa opioid receptor antagonist is a  
compound of formula (I), wherein R<sub>1</sub>, R<sub>4</sub>, R<sub>5</sub>, Y<sub>1</sub>, Y<sub>2</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub>, and R<sub>7</sub>-R<sub>17</sub> are as indicated  
above;

Y<sub>3</sub> is H;

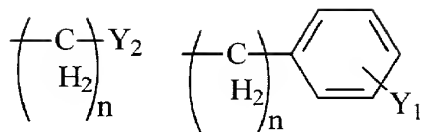
R<sub>2</sub> and R<sub>3</sub> are each, independently, H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, CH<sub>2</sub> aryl  
substituted by one or more substituents Y<sub>1</sub>; and

R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a)-  
(cc).

and pharmaceutically acceptable salts thereof.

3. The method of claim 1, wherein said kappa opioid receptor antagonist is a  
compound of formula (I) wherein Y<sub>1</sub>, Y<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>15</sub> are as indicated  
above;

R<sub>1</sub> is C<sub>1-8</sub> alkyl,



$\text{Y}_3$  is H;

$\text{R}_2$  and  $\text{R}_3$  are each, independently, H or  $\text{C}_{1-8}$  alkyl, wherein  $\text{R}_2$  and  $\text{R}_3$  cannot both be H at the same time;

$\text{R}_6$  is a formula selected from the structures (a)-(r); and

$\text{R}_7$  is H,  $\text{C}_{1-8}$  alkyl,  $\text{CH}_2$ aryl substituted by one or more substituents  $\text{Y}_1$ ,  $\text{NR}_{10}\text{R}_{11}$ ,  $\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{13}$ ,  $\text{CONR}_{14}\text{R}_{15}$ , or  $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$ .

4. The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein  $\text{Y}_1$ , Z, n,  $\text{X}_1$ ,  $\text{X}_2$  and  $\text{R}_8\text{-R}_{15}$  are as noted above;

$\text{R}_1$  is  $\text{C}_{1-8}$  alkyl;

$\text{Y}_2$  is H,  $\text{CF}_3$ ,  $\text{CO}_2\text{R}_9$ ,  $\text{C}_{1-6}$  alkyl,  $\text{NR}_{10}\text{R}_{11}$ ,  $\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{12}$ ,  $\text{CONR}_{13}\text{R}_{14}$ ,  $\text{CH}_2\text{OH}$ ,  $\text{CH}_2\text{OR}_8$ ,  $\text{COCH}_2\text{R}_9$ ;

$\text{Y}_3$  is H;

$\text{R}_2$  and  $\text{R}_3$  are each, independently, H or methyl, wherein  $\text{R}_2$  and  $\text{R}_3$  cannot both be H at the same time;

$\text{R}_4$  is H,  $\text{C}_{1-8}$  alkyl,  $\text{CO}_2\text{C}_{1-8}$ alkyl, aryl substituted by one or more substituents  $\text{Y}_1$  and the stereocenter adjacent to  $\text{R}_4$  is in an (S) configuration;

$\text{R}_5$  is H,  $\text{C}_{1-8}$  alkyl,  $\text{CH}_2\text{CO}_2\text{C}_{1-8}$  alkyl;

$\text{R}_6$  is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

$\text{R}_7$  is H,  $\text{C}_{1-8}$ alkyl,  $\text{CH}_2$ aryl substituted by one or more substituents  $\text{Y}_1$ ,  $\text{NR}_{10}\text{R}_{11}$ ,  $\text{NHCOR}_{12}$ ,  $\text{NHCO}_2\text{R}_{13}$ ,  $\text{CONR}_{14}\text{R}_{15}$ , or  $\text{CH}_2(\text{CH}_2)_n\text{Y}_2$ .

5. The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein  $\text{Y}_1$ , Z, n,  $\text{X}_1$ ,  $\text{X}_2$  and  $\text{R}_8\text{-R}_{14}$  are as indicated above;

R<sub>1</sub> is methyl,

Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>,  
CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, COCH<sub>2</sub>R<sub>9</sub>;

Y<sub>3</sub> is H;

5 R<sub>2</sub> and R<sub>3</sub> are each H or methyl, such that when R<sub>2</sub> is H, R<sub>3</sub> is methyl and vice versa;  
R<sub>4</sub> is C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkyl, and the stereocenter adjacent to R<sub>4</sub> has a configuration  
of (S);

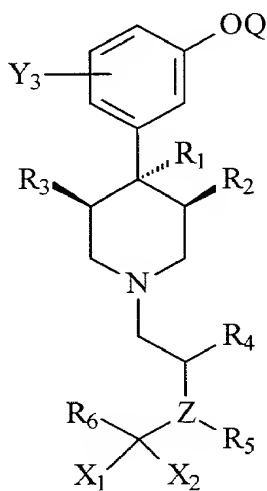
R<sub>5</sub> is H;

10 R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a) and  
(b); and

R<sub>7</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub> or  
CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

6. The method of claim 1, wherein said kappa opioid receptor antagonist is a  
compound selected from formulae **14-21** of Fig. 1.

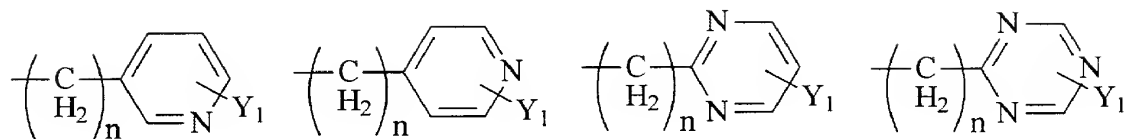
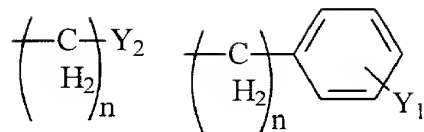
7. A kappa opioid receptor antagonist compound represented by the formula (I):



(I)

wherein Q is H or COC<sub>1-8</sub> alkyl;

R<sub>1</sub> is C<sub>1-8</sub> alkyl, or one of the following structures:



Y<sub>1</sub> is H, OH, Br, Cl, F, CN, CF<sub>3</sub>, NO<sub>2</sub>, N<sub>3</sub>, OR<sub>8</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub>alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, COCH<sub>2</sub>R<sub>9</sub>;

Y<sub>3</sub> is H, OH, Br, Cl, F, CN, CF<sub>3</sub>, NO<sub>2</sub>, N<sub>3</sub>, OR<sub>8</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

R<sub>2</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>;

R<sub>3</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>,

wherein R<sub>2</sub> and R<sub>3</sub> may be bonded together to form a C<sub>2-8</sub> alkyl group;

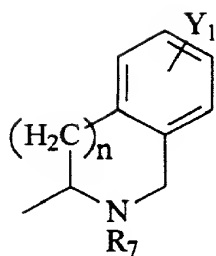
R<sub>4</sub> is hydrogen, C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkylaryl substituted by one or more groups Y<sub>1</sub>, CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub> or CO<sub>2</sub>C<sub>1-8</sub> alkyl;

Z is N, O or S; when Z is O or S there is no R<sub>5</sub>

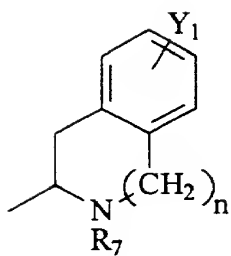
15 R<sub>5</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, CH<sub>2</sub>CO<sub>2</sub>C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>;

n is 0, 1, 2 or 3;

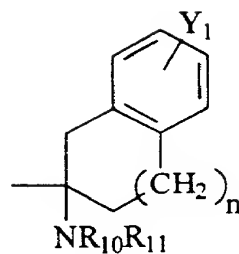
R<sub>6</sub> is a group selected from the group consisting of structures (a)-(bbb):



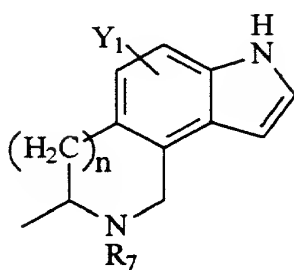
(a)



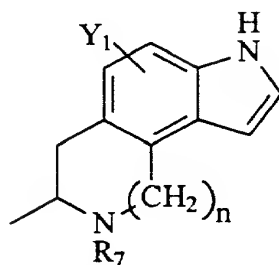
(b)



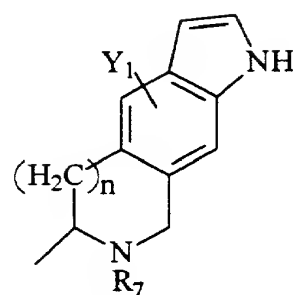
(c)



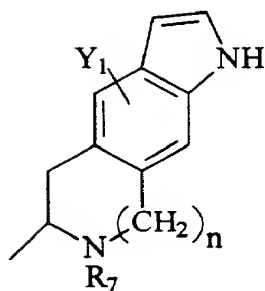
(d)



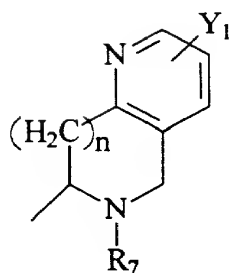
(e)



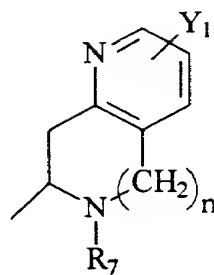
(f)



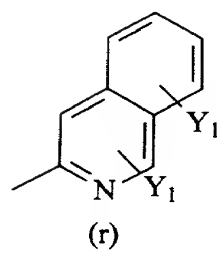
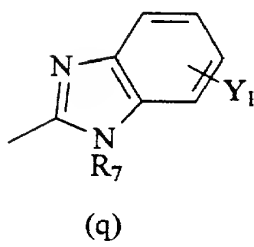
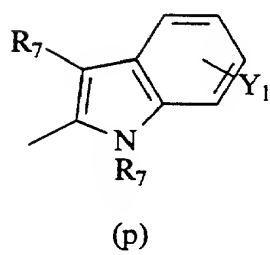
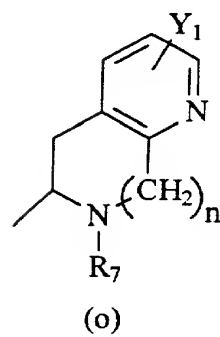
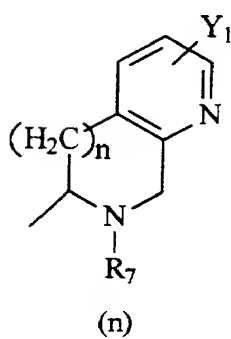
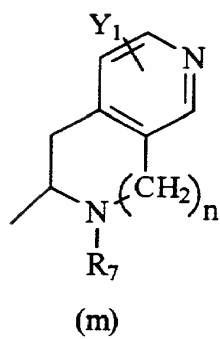
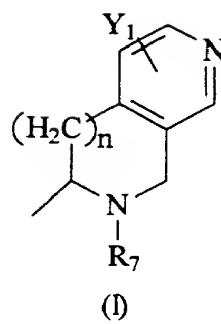
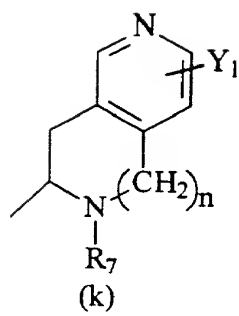
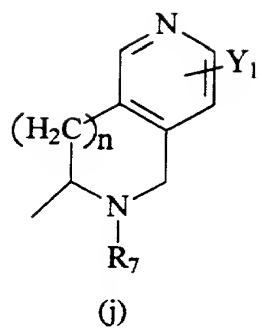
(g)

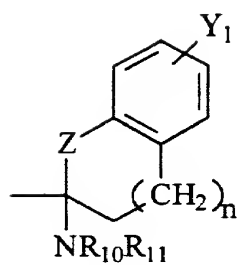


(h)

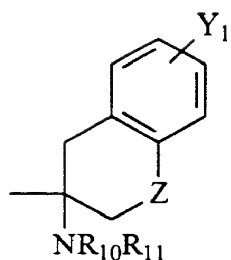


(i)

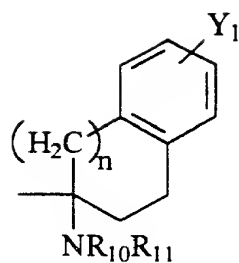




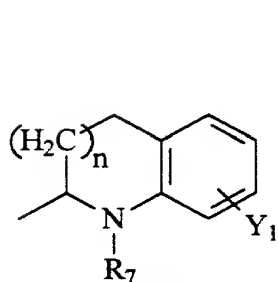
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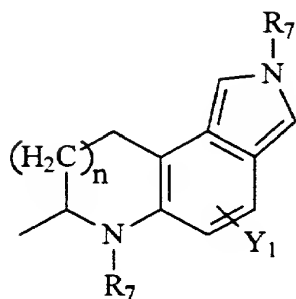
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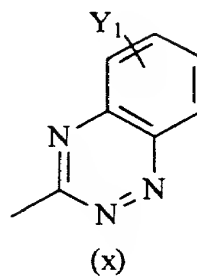
(u)



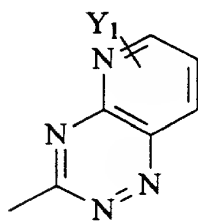
(v)



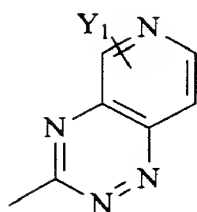
(w)



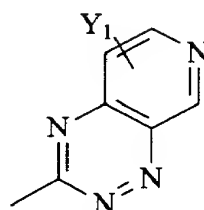
(x)



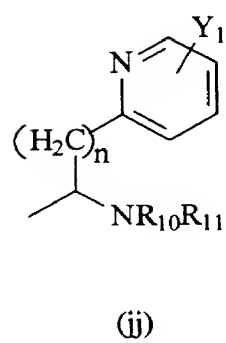
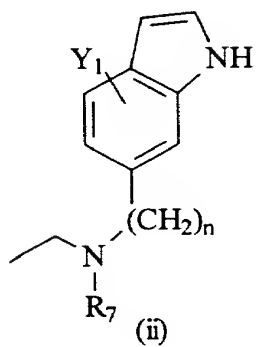
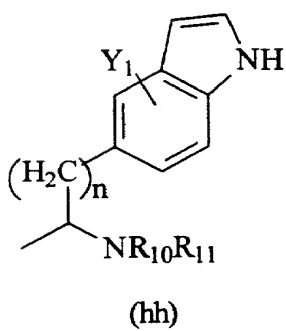
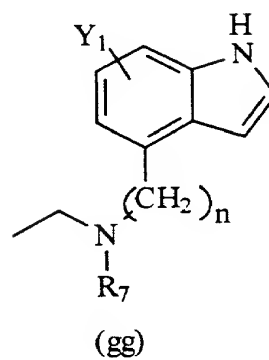
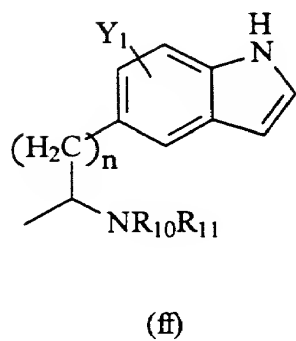
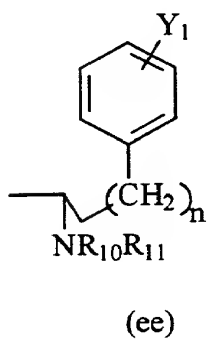
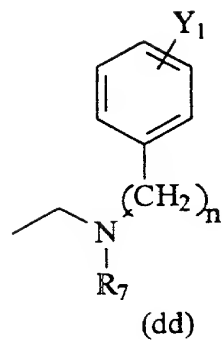
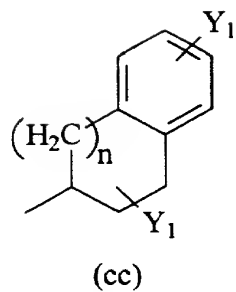
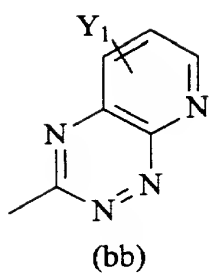
(y)



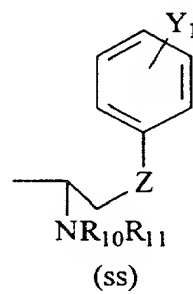
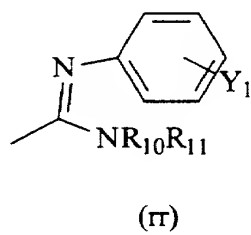
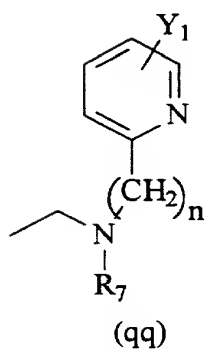
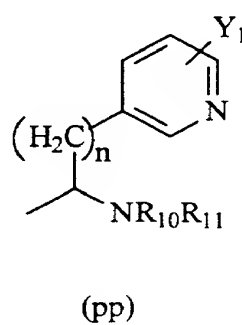
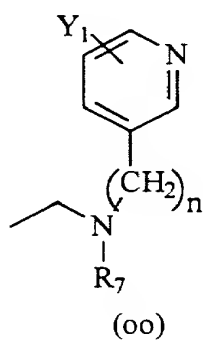
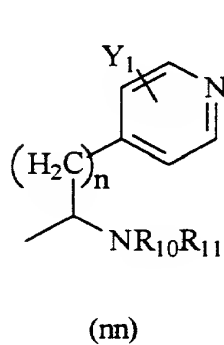
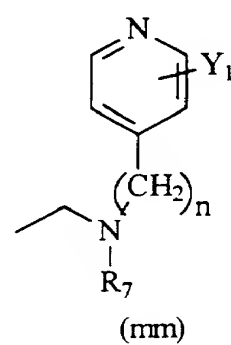
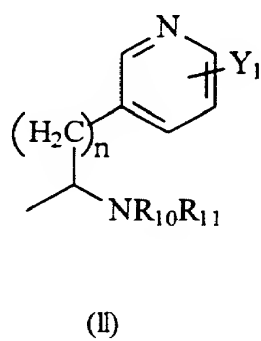
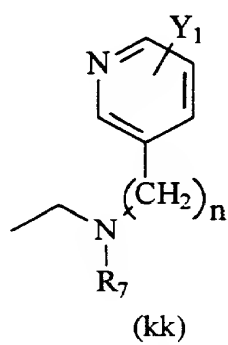
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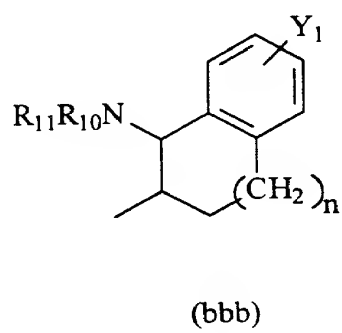
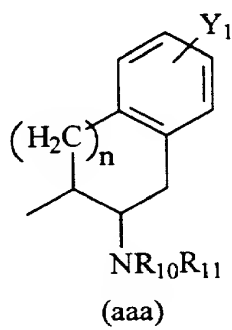
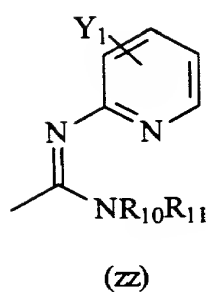
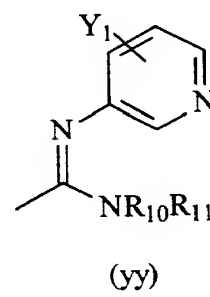
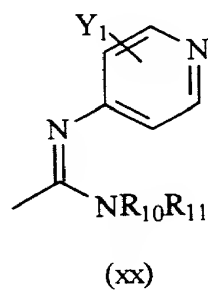
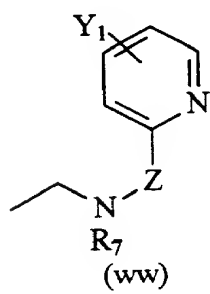
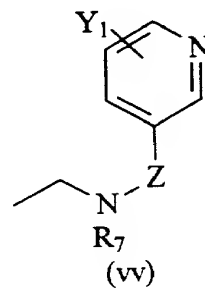
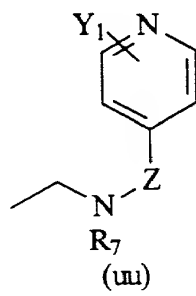
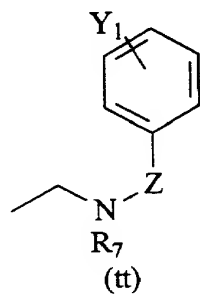


(aa)









X<sub>1</sub> is hydrogen, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl;

X<sub>2</sub> is hydrogen, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl;

or X<sub>1</sub> and X<sub>2</sub> together form =O, =S, =NH;

R<sub>7</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>,

5 NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>, C(=NH)NR<sub>16</sub>R<sub>17</sub>,

R<sub>8</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CONR<sub>13</sub>R<sub>14</sub>,

CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>9</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

R<sub>10</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

10 R<sub>11</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>12</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>13</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>14</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>15</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>16</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

and

R<sub>17</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>  
and pharmaceutically acceptable salts thereof.

8. The kappa opioid receptor antagonist compound of claim 7, wherein R<sub>1</sub>, R<sub>4</sub>, R<sub>5</sub>, Y<sub>1</sub>,  
20 Y<sub>2</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub>, and R<sub>7</sub>-R<sub>17</sub> are as indicated above;

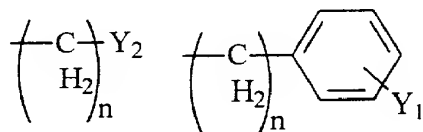
Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each, independently, H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, CH<sub>2</sub> aryl  
substituted by one or more substituents Y<sub>1</sub>; and

R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a)-  
25 (cc).

9. The kappa opioid receptor antagonist compound of claim 7, wherein Y<sub>1</sub>, Y<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>,  
Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>15</sub> are as indicated above;

R<sub>1</sub> is C<sub>1-8</sub> alkyl,



Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each, independently, H or C<sub>1-8</sub> alkyl, wherein R<sub>2</sub> and R<sub>3</sub> cannot both be H at the same time;

R<sub>6</sub> is a formula selected from the structures (a)-(r) shown above; and

5 R<sub>7</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

10. The kappa opioid receptor antagonist compound of claim 7, wherein Y<sub>1</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>15</sub> are as noted above;

R<sub>1</sub> is C<sub>1-8</sub> alkyl;

10 Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, COCH<sub>2</sub>R<sub>9</sub>;

Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each, independently, H or methyl, wherein R<sub>2</sub> and R<sub>3</sub> cannot both be H at the same time;

15 R<sub>4</sub> is H, C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub>alkyl, aryl substituted by one or more substituents Y<sub>1</sub> and the stereocenter adjacent to R<sub>4</sub> is in an (S) configuration;

R<sub>5</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>CO<sub>2</sub>C<sub>1-8</sub> alkyl;

R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

20 R<sub>7</sub> is H, C<sub>1-8</sub>alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

11. The kappa opioid receptor antagonist compound of claim 7, wherein Y<sub>1</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>14</sub> are as indicated above;

R<sub>1</sub> is methyl,

25 Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, COCH<sub>2</sub>R<sub>9</sub>;

Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each H or methyl, such that when R<sub>2</sub> is H, R<sub>3</sub> is methyl and vice versa;

$R_4$  is  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkyl, and the stereocenter adjacent to  $R_4$  has a configuration of (S);

$R_5$  is H;

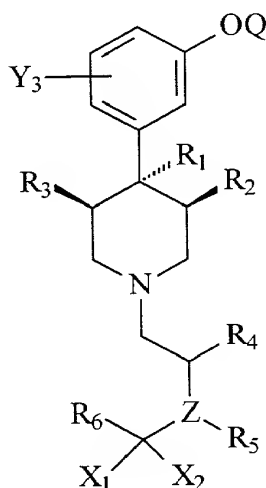
$R_6$  is a group having a formula selected from the group consisting of structures (a) and (b); and

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$  or  $CH_2(CH_2)_nY_2$ .

12. The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae **14-21** of Fig. 1.

13. A pharmaceutical composition comprising:

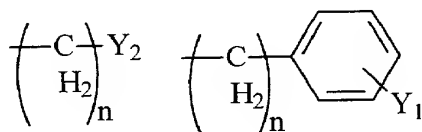
an effective amount of a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):

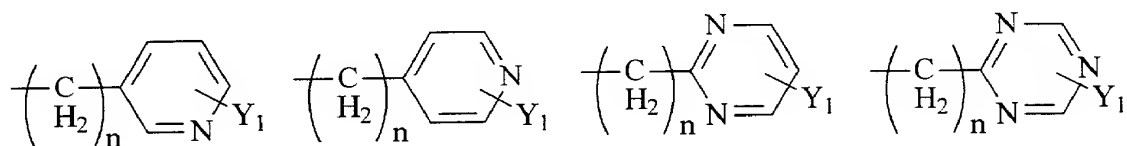


(I)

wherein Q is H or  $CO_2C_{1-8}$  alkyl;

$R_1$  is  $C_{1-8}$  alkyl, or one of the following structures:





Y<sub>1</sub> is H, OH, Br, Cl, F, CN, CF<sub>3</sub>, NO<sub>2</sub>, N<sub>3</sub>, OR<sub>8</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub>alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, COCH<sub>2</sub>R<sub>9</sub>;

5  $Y_3$  is H, OH, Br, Cl, F, CN,  $CF_3$ ,  $NO_2$ ,  $N_3$ ,  $OR_8$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCOR_{12}$ ,  
 $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,  $CH_2(CH_2)_nY_2$ ;

R<sub>2</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>;

R<sub>3</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>.

wherein R<sub>2</sub> and R<sub>3</sub> may be bonded together to form a C<sub>2-8</sub> alkyl group;

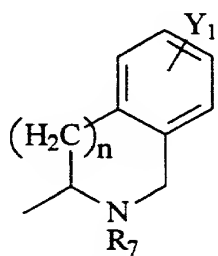
R<sub>4</sub> is hydrogen, C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkylaryl substituted by one or more groups Y<sub>1</sub>, CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>, or CO<sub>2</sub>C<sub>1-8</sub> alkyl;

$Z$  is N, O or S; when  $Z$  is O or S, there is no  $R_5$

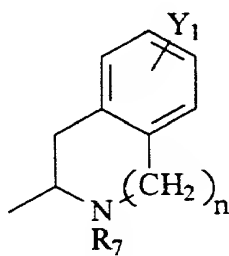
R<sub>5</sub> is H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, CH<sub>2</sub>CO<sub>2</sub>C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub> alkyl or CH<sub>2</sub>aryl substituted by one or more groups Y<sub>1</sub>;

$n$  is 0, 1, 2 or 3;

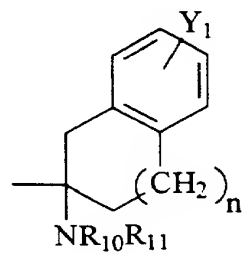
$R_6$  is a group selected from the group consisting of structures (a)-(bbb):



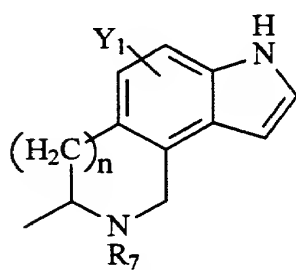
(a)



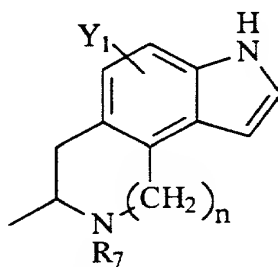
(b)



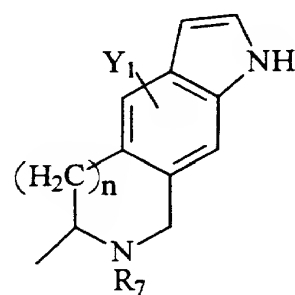
(c)



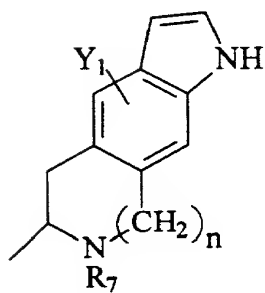
(d)



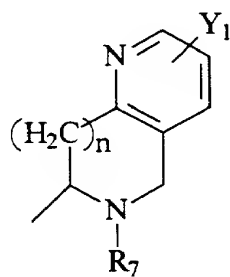
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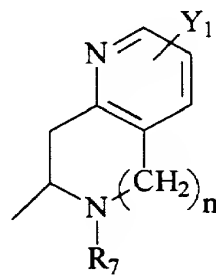
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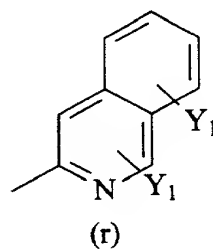
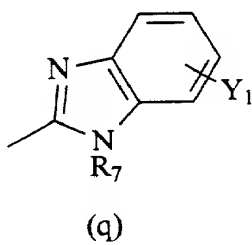
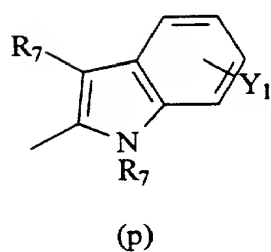
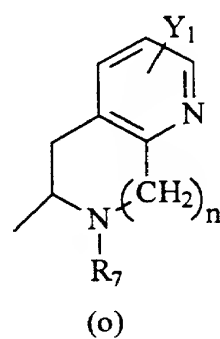
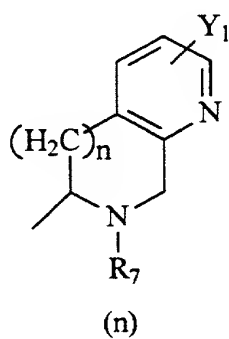
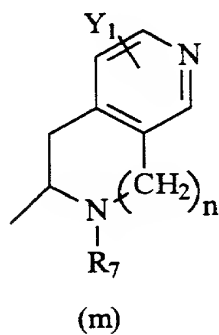
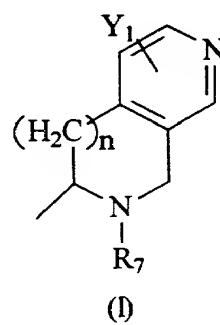
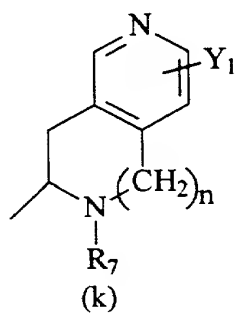
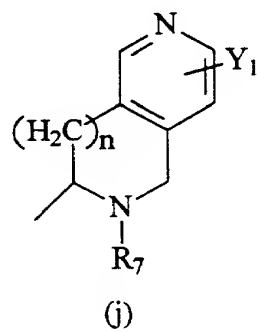
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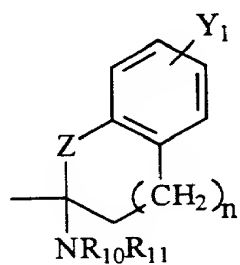
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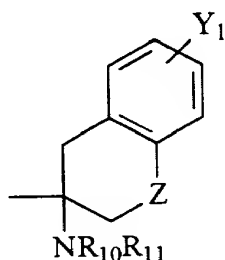
(i)



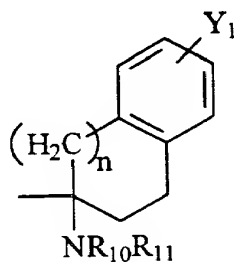




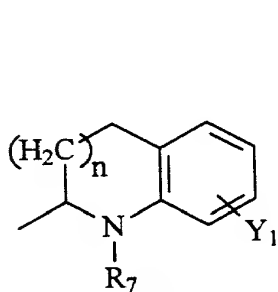
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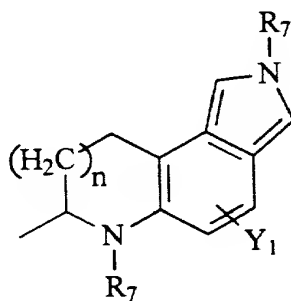
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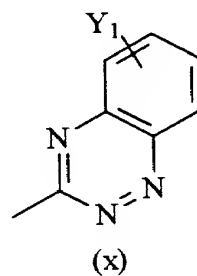
(u)



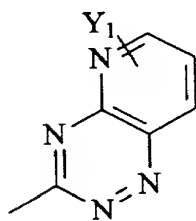
(v)



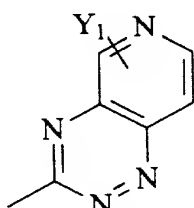
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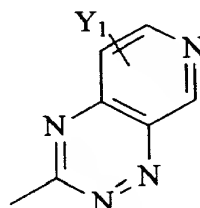
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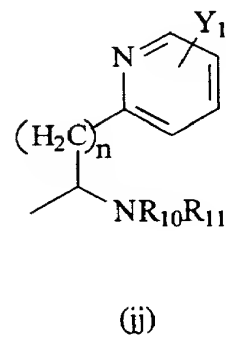
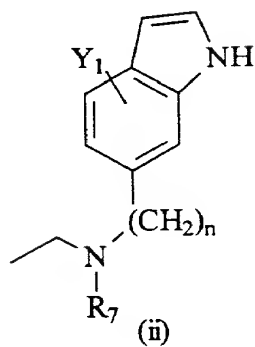
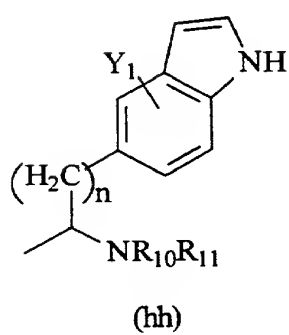
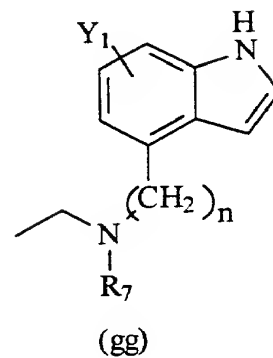
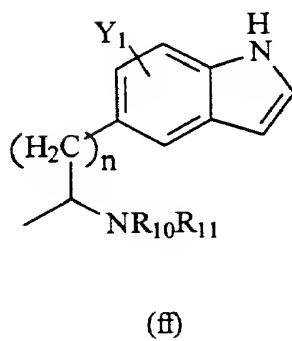
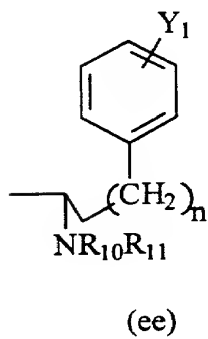
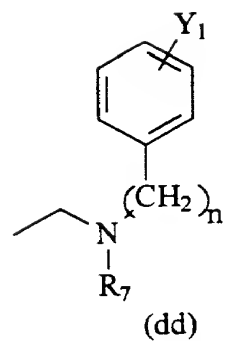
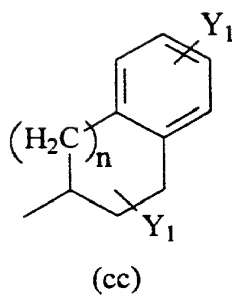
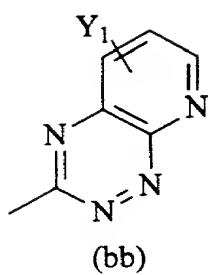
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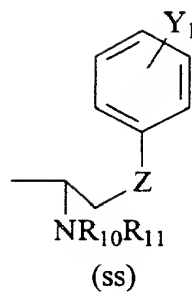
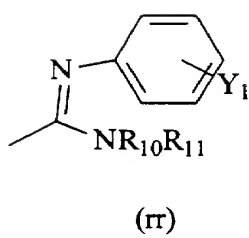
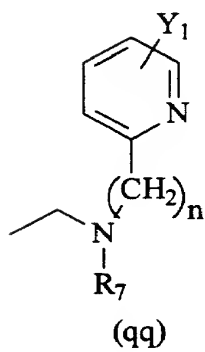
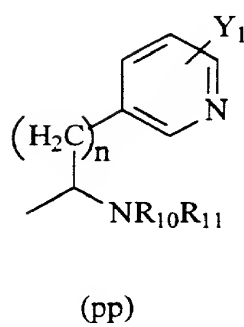
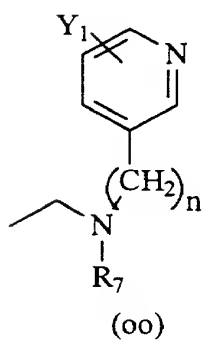
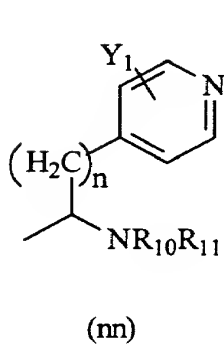
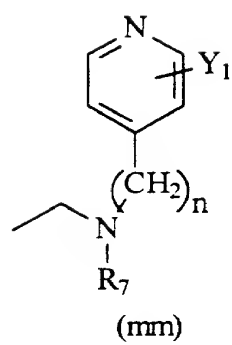
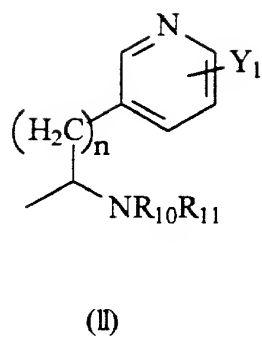
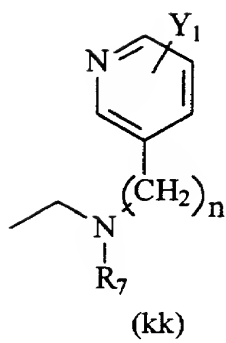


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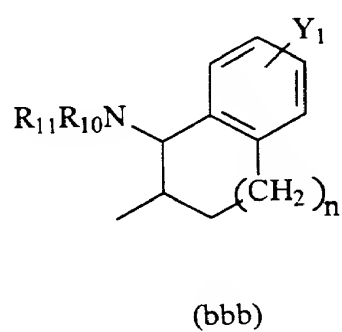
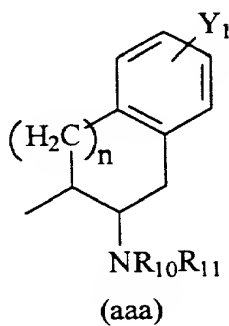
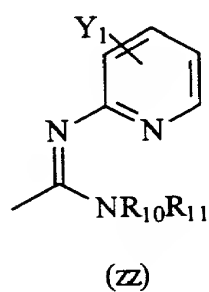
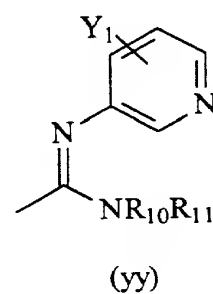
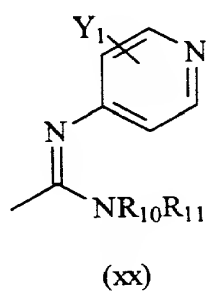
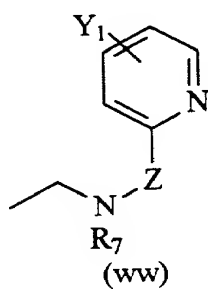
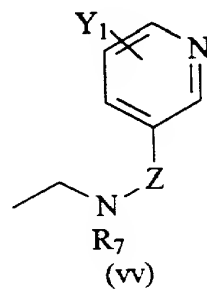
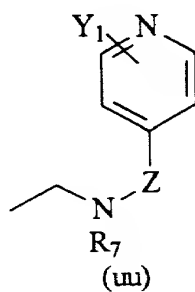
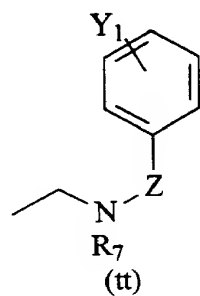


(aa)





Parameter	Value	Unit
Initial concentration	1.0	g/L
Initial pH	7.0	
Temperature	25	°C
Time	0-120	min
Agitation speed	150	rpm
Batch size	100	mL
Adsorbent dose	0.1-1.0	g/L
Adsorbent type	Activated carbon	
Adsorbent surface area	1000	m <sup>2</sup> /g
Adsorbent pore volume	0.5	cm <sup>3</sup> /g
Adsorbent density	0.5	g/cm <sup>3</sup>
Adsorbent particle size	0.15-0.25	mm
Adsorbent batch	1	
Adsorbent source	Commercial	
Adsorbent treatment	None	
Adsorbent storage	Room temperature	
Adsorbent handling	Standard	
Adsorbent disposal	Standard	
Adsorbent reuse	Standard	
Adsorbent regeneration	Standard	
Adsorbent monitoring	Standard	
Adsorbent maintenance	Standard	
Adsorbent safety	Standard	
Adsorbent quality	Standard	
Adsorbent quantity	Standard	
Adsorbent quality control	Standard	
Adsorbent quantity control	Standard	
Adsorbent quality assurance	Standard	
Adsorbent quantity assurance	Standard	
Adsorbent quality management	Standard	
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Adsorbent quantity collaboration	Standard	
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Adsorbent quantity consortium	Standard	
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Adsorbent quantity network	Standard	
Adsorbent quality community	Standard	
Adsorbent quantity community	Standard	
Adsorbent quality association	Standard	
Adsorbent quantity association	Standard	
Adsorbent quality organization	Standard	
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Adsorbent quantity zone	Standard	
Adsorbent quality point	Standard	
Adsorbent quantity point	Standard	
Adsorbent quality line	Standard	
Adsorbent quantity line	Standard	
Adsorbent quality surface	Standard	
Adsorbent quantity surface	Standard	
Adsorbent quality volume	Standard	
Adsorbent quantity volume	Standard	
Adsorbent quality mass	Standard	
Adsorbent quantity mass	Standard	
Adsorbent quality weight		



X<sub>1</sub> is hydrogen, C<sub>1-8</sub> alkyl, C<sub>3-8</sub>alkenyl, C<sub>3-8</sub>alkynyl;

X<sub>2</sub> is hydrogen, C<sub>1-8</sub>alkyl, C<sub>3-8</sub>alkenyl, C<sub>3-8</sub>alkynyl;

or X<sub>1</sub> and X<sub>2</sub> together form =O, =S, =NH;

R<sub>7</sub> is H, C<sub>1-8</sub>alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>,

5 NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>, C(=NH)NR<sub>16</sub>R<sub>17</sub>.

R<sub>8</sub> is H, C<sub>1-8</sub>alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, CONR<sub>13</sub>R<sub>14</sub>,

CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>9</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>;

R<sub>10</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

10 R<sub>11</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>12</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>13</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>14</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

R<sub>15</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

15 R<sub>16</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

and

R<sub>17</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub> aryl substituted by one or more substituents Y<sub>1</sub>, CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>

or a pharmaceutically acceptable salt thereof.

14. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor  
20 antagonist is a compound of formula (I), wherein R<sub>1</sub>, R<sub>4</sub>, R<sub>5</sub>, Y<sub>1</sub>, Y<sub>2</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub>, and R<sub>7</sub>-R<sub>17</sub>  
are as indicated above;

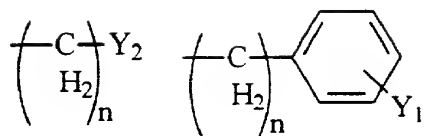
Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each, independently, H, C<sub>1-8</sub> alkyl, C<sub>3-8</sub> alkenyl, C<sub>3-8</sub> alkynyl, CH<sub>2</sub>aryl  
substituted by one or more substituents Y<sub>1</sub>; and

25 R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a)-  
(cc).

15. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor  
antagonist is a compound of formula (I), wherein Y<sub>1</sub>, Y<sub>2</sub>, R<sub>4</sub>, R<sub>5</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>15</sub> are as  
indicated above;

30 R<sub>1</sub> is C<sub>1-8</sub> alkyl,



Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each, independently, H or C<sub>1-8</sub> alkyl, wherein R<sub>2</sub> and R<sub>3</sub> cannot both be H at the same time;

R<sub>6</sub> is a formula selected from the structures (a)-(r) shown above; and

R<sub>7</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

16. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y<sub>1</sub>, Z, n, X<sub>1</sub>, X<sub>2</sub> and R<sub>8</sub>-R<sub>15</sub> are as noted above;

R<sub>1</sub> is C<sub>1-8</sub> alkyl;

Y<sub>2</sub> is H, CF<sub>3</sub>, CO<sub>2</sub>R<sub>9</sub>, C<sub>1-6</sub> alkyl, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>12</sub>, CONR<sub>13</sub>R<sub>14</sub>, CH<sub>2</sub>OH, CH<sub>2</sub>OR<sub>8</sub>, COCH<sub>2</sub>R<sub>9</sub>;

Y<sub>3</sub> is H;

R<sub>2</sub> and R<sub>3</sub> are each, independently, H or methyl, wherein R<sub>2</sub> and R<sub>3</sub> cannot both be H at the same time;

R<sub>4</sub> is H, C<sub>1-8</sub> alkyl, CO<sub>2</sub>C<sub>1-8</sub>alkyl, aryl substituted by one or more substituents Y<sub>1</sub> and the stereocenter adjacent to R<sub>4</sub> is in an (S) configuration;

R<sub>5</sub> is H, C<sub>1-8</sub> alkyl, CH<sub>2</sub>CO<sub>2</sub>C<sub>1-8</sub> alkyl;

R<sub>6</sub> is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R<sub>7</sub> is H, C<sub>1-8</sub>alkyl, CH<sub>2</sub>aryl substituted by one or more substituents Y<sub>1</sub>, NR<sub>10</sub>R<sub>11</sub>, NHCOR<sub>12</sub>, NHCO<sub>2</sub>R<sub>13</sub>, CONR<sub>14</sub>R<sub>15</sub>, or CH<sub>2</sub>(CH<sub>2</sub>)<sub>n</sub>Y<sub>2</sub>.

17. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein  $Y_1$ ,  $Z$ ,  $n$ ,  $X_1$ ,  $X_2$  and  $R_8$ - $R_{14}$  are as indicated above;

$R_1$  is methyl,

$Y_2$  is H,  $CF_3$ ,  $CO_2R_9$ ,  $C_{1-6}$  alkyl,  $NR_{10}R_{11}$ ,  $NHCO_2R_{12}$ ,  $CONR_{13}R_{14}$ ,  $CH_2OH$ ,  $CH_2OR_8$ ,  $COCH_2R_9$ ;

$Y_3$  is H;

$R_2$  and  $R_3$  are each H or methyl, such that when  $R_2$  is H,  $R_3$  is methyl and vice versa;

$R_4$  is  $C_{1-8}$  alkyl,  $CO_2C_{1-8}$  alkyl, and the stereocenter adjacent to  $R_4$  has a configuration of (S);

$R_5$  is H;

$R_6$  is a group having a formula selected from the group consisting of structures (a) and (b); and

$R_7$  is H,  $C_{1-8}$  alkyl,  $CH_2$ aryl substituted by one or more substituents  $Y_1$  or  $CH_2(CH_2)_nY_2$ .

18. The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 of Fig. 1.

19. The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

20. The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

21. The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.